GENES VII

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CHAPTER 27

Nucleosomes

Chromatin has a compact organization in which most DNA sequences are structurally inaccessible and functionally inactive. Within this mass are the minority of active sequences. What is the general structure of chromatin, and what is the difference between active and inactive sequences? The high overall packing ratio of the genetic material immediately suggests that DNA cannot be directly packaged into the final structure of chromatin. There must be *hierarchies* of organization.

The fundamental subunit of chromatin has the same type of design in all eukaryotes. The nucleosome contains ~200 bp of DNA, organized by an octamer of small, basic proteins in a bead-like structure. The protein components are **histones.** They form an interior core; DNA lies on the surface of the particle. Nucleosomes are an invariant component of euchromatin and heterochromatin in the interphase nucleus, and of mitotic chromosomes. The formation of the nucleosome forms the first level of organization, giving a packing ratio of ~6. The components and structure of the nucleosome are well characterized.

The second level of organization is the coiling of the series of nucleosomes into a helical fiber to constitute the ~30 nm fiber that is found in both interphase chromatin and mitotic chromosomes (see Figure 26.8). In chromatin this gives the packing ratio of DNA to ~40. The structure of this fiber requires additional proteins but is not well defined.

The overall packing ratio is determined by the third level of organization, the packaging of the fiber itself. This gives an overall packing ratio of ~1000 in euchromatin, cyclically interchangeable with packing into mitotic chromosomes to achieve an overall ratio of ~10,000. A similar increase in condensation is seen in heterochromatin.

We need to work through these levels of organization to characterize the events involved in cyclical packaging, replication, and transcription. We assume that association with additional proteins, or modifications of existing chromosomal proteins, are involved in changing the structure of chromatin. We do not know the individual targets for controlling cyclical packaging. Both replication and transcription require unwinding of DNA, and thus must involve an unfolding of the structure that allows the relevant enzymes to manipulate the DNA. This is likely to involve changes in all levels of organization, but at present these processes can be characterized only in terms of changes at the level of the nucleosomes.

When chromatin is replicated, the nucleosomes must be reproduced on both daughter duplex molecules. As well as asking how the nucleosome itself is assembled, we must inquire what happens to other proteins present in chromatin. Since replication disrupts the structure of chromatin, it both poses a problem for maintaining regions with specific structure and offers an opportunity to change the structure.

The mass of chromatin contains up to twice as much protein as DNA. Approximately half of the protein mass is accounted for by the nucleosomes. The mass of RNA is less than 10% of the mass of DNA. Much of the RNA consists